REMARKS

A number of claims have been amended to replace the terms "has" with "consists of". Applicants view the term "has" in this context as being synonymous with "consists of". Also, minor typographical errors have been amended. These changes are intended to make the language of the claims more consistent and definite, and do not narrow the original scope of the claims so amended.

No new matter has been added by the amendments to the specification or by the new claims. Therefore, their entry into the present application is respectfully requested.

In paper #10, dated March 21, 2003, the Examiner imposed two restriction requirements.

The first restricts the application to one of two inventions. Group I, containing claims 1-19 and 41-46, is drawn to methods of stimulating bone growth using a therapeutically effective amount of a physiologically functional equivalent thrombin derivative peptide. Group II, containing claims 20-40, is drawn to pharmaceutical compositions comprising a therapeutically effective amount of a physiologically functional equivalent thrombin derivative peptide . The Examiner states Groups I and II are related as product and process of use.

The second restricts the application to a single peptide. The Examiner states:

> Amino acid sequences are also structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constituted independent and distinct inventions.

The Examiner also stated:

> Accordingly, only one (1) independent and distinct nucleotide/polypeptide sequence in a single application will be examined without restriction.

The Second Restriction Requirement is traversed.

The claimed invention is a method of treatment in which the therapeutically active agent is generically described. The Examiner is apparently asserting that only one species within this generic claim will be examined because the genus allegedly contains species which are independent and distinct.

Applicants' Attorney has never received a Restriction Requirement of this type. Surely, most generic claims contain species which are independent and distinct. It does not follow that the Examiner can properly "carve up" the genus and restrict within it. It would be unduly burdensome to require an applicant to individually prosecute every species within a genus. More importantly, it is contrary to Patent Office Policy, as enunciated in the MPEP.

> There are a number of situations which arise in which an application has claims to two or more properly divisible inventions, so that a requirement to restrict the application to one would be proper, but presented in the same case are one or more claims (generally called "linking" claims) inseparable therefrom and thus linking together the inventions otherwise divisible. The most common types of linking claims which, if allowed, **act to prevent restriction** between inventions that can otherwise be shown to be divisible, are (A) **genus claims linking species claims**. (MPEP 809.03).

The claims of the instant application are inseparable from numerous linking claims, e.g., independent Claim 1, drawn in part to "an agonist of the non-proteolytically activated thrombin receptor". **Each claim in the instant application is drawn, at least in part, to a species contained within the genus defined by Claim 1**. Thus, Claim 1 **links** the claims and **acts to prevent restriction** between them. Therefore, the second restriction is improper and Applicants respectfully request that the restriction be withdrawn. In making these statements, Applicants in no way admit that the groups would be properly divisible if the linking claim were not present.

If the Examiner feels that a search to the genus of Claim 1 would be unduly burdensome, the MPEP provides a procedure for election of species:

> Election of species should be required prior to a search on the merits (A) in all applications containing claims to a plurality of species with no generic claims, and (B) in all applications containing both species claims and ***generic*** or Markush claims. In all applications in which no species claims are present and a ***generic*** claim recites such a multiplicity of species that an unduly extensive and burdensome search is required, a requirement for an election of species should be made prior to a search of the generic claim. MPEP §808.01(a). (Emphasis added).

The elected species should be searched, and, if no invalidating prior art found, the search should be extended to cover non-elected species until the entire scope of the claims have been searched, in accordance with the procedure set forth in MPEP §809.02.

Should the second restriction be withdrawn and replaced with a requirement for election of species, Applicant hereby elects Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-$CONH_2$ (SEQ ID NO: 6). as the species. Claims readable on the elected species include Claims 1-46, as amended.

Responsive to the first Restriction Requirement dated March 21, 2003, the claims of Group I (Claims 1-19 and 41-46) drawn to methods of stimulating bone growth using an agonist of the non-proteolytically activated thrombin receptor are elected for prosecution. Responsive to the second Restriction Requirement dated March 21, 2003, Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-$CONH_2$ (SEQ ID NO: 6). is the species elected for prosecution. Applicant reserve the right to file a continuing application or take such other appropriate action as deemed necessary to protect the non-elected inventions. Applicant does not hereby abandon or waive any rights in the non-elected inventions.

CONCLUSION

Claims 1-46 are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By _____

Steven G. Davis
Registration No.: 39,652
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133

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MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

5. (Amended) The method of Claim 4 wherein the thrombin peptide derivative consists of[has] between about 12 and about 23 amino acids.

6. (Amended) The method of Claim 5 wherein the serine esterase conserved sequence consists of[has] the amino acid sequence of SEQ ID NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a *C*-terminal truncated fragment thereof having at least six amino acids, provided that zero, one, two or three amino acids in the serine esterase conserved sequence differ from the corresponding position of SEQ ID NO 1.

7. (Amended) The method of Claim 5 wherein the serine esterase conserved sequence consists of[has] the amino acid sequence of SEQ ID NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a *C*-terminal truncated fragment thereof having at least nine amino acids, provided that zero, one or two of the amino acids in the serine esterase conserved region are conservative substitutions[susbstitutions] of the corresponding amino acid in SEQ ID NO 1.

8. (Amended) The method of Claim 5 wherein the serine esterase conserved sequence consists of[has] the amino acid sequence of SEQ ID NO 2 (Cys-X_1-Gly-Asp-Ser-Gly-Gly-Pro-X_2-Val, wherein X_1 is Glu or Gln and X_2 is Phe, Met, Leu, His or Val), or a *C*-terminus truncated fragment of SEQ ID NO 2, said fragment having at least six amino acids.

11. (Amended) The method of Claim 10 wherein the thrombin peptide derivative consists of[has] the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- (SEQ ID NO 5), or an *N*-terminal truncated fragment thereof, provided that zero, one, two or three amino acids at positions 1-9 in the thrombin peptide derivative differ from the amino acid at the corresponding position of SEQ ID NO 5.

12. (Amended) The method of Claim 10 wherein the thrombin peptide derivative consists of[has] the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- (SEQ ID NO 5), or an *N*-terminal truncated fragment thereof, provided that zero, one or two amino acids at positions 1-9 in the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO 5.

14. (Amended) The method of Claim 5, wherein the subject is administered a therapeutically effective amount of a physiologically functional equivalent thrombin derivative peptide [comprising]of the sequence Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-$CONH_2$ (SEQ ID NO: 6).

22. (Amended) The pharmaceutical composition of Claim 21 wherein the thrombin receptor agonist is a thrombin peptide derivative [comprises]comprising a polypeptide represented by the following structural formula or a physiologically functional equivalent thereof:

Asp-Ala-R;

wherein R is a serine esterase conserved sequence.

30. (Amended) The pharmaceutical composition of Claim 22 wherein the thrombin peptide derivative consists of[has] between about 12 and about 23 amino acids.

31. (Amended) The pharmaceutical composition of Claim 30 wherein the serine esterase conserved sequence consists of[has] the amino acid sequence of SEQ ID NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a *C*-terminal truncated fragment thereof having at least six amino acids, provided that zero, one, two or three amino acids in the serine esterase conserved sequence differ from the corresponding position of SEQ ID NO 1.

32. (Amended) The pharmaceutical composition of Claim 30 wherein the serine esterase conserved sequence consists of[has] the amino acid sequence of SEQ ID NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a *C*-terminal truncated fragment thereof having at least nine amino acids, provided that zero, one or two of the amino acids in the serine esterase conserved sequence are conservative substitutions[susbstitutions] of the corresponding amino acid in SEQ ID NO 1.

33. (Amended) The pharmaceutical composition of Claim 30 wherein the serine esterase conserved sequence consists of[has] the amino acid sequence of SEQ ID NO 2 (Cys-X_1-Gly-Asp-Ser-Gly-Gly-Pro-X_2-Val) , wherein X_1 is Glu or Gln and X_2 is Phe, Met, Leu, His or Val), or a *C*-terminus truncated fragment of SEQ ID NO 2, said fragment having at least six amino acids.

36. (Amended) The pharmaceutical composition of Claim 35 wherein the thrombin peptide derivative consists of[has] the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- (SEQ ID NO 5), or an *N*-terminal truncated fragment thereof, provided that zero, one, two or three amino acids at positions 1-9 in the thrombin peptide derivative differ from the amino acid at the corresponding position of SEQ ID NO 5.

37. (Amended) The pharmaceutical composition of Claim 35 wherein the thrombin peptide derivative consists of[has] the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- (SEQ ID NO 5), or an *N*-terminal truncated fragment thereof, provided that zero, one or two amino acids at positions 1-9 in the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO 5.

43. (Amended) A method of stimulating bone growth in a subject at a segmental bone gap, a bone void or a non-union fracture[facture], said method comprising the step of administering to the bone gap, bone void or nonunion fracture,[facture] a therapeutically effective amount of a peptide having the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO 5).